IMPACT OF UNTREATED ADOLESCENT IDIOPATHIC SCOLIOSIS IN ADULTHOOD: A TEN-YEAR ANALYSIS

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Abstract

Title: Impact of Untreated Adolescent Idiopathic Scoliosis in Adulthood: A Ten-Year Analysis

Background: Long-term studies of adolescent idiopathic scoliosis (AIS) in adulthood demonstrate most patients function well, though some have increased disability. The Oswestry Disability Index (ODI) and SRS-22r are validated questionnaires for assessing back disability and quality of life respectively. Our purpose was to further establish the impact of untreated AIS in adulthood. The rationale for this project was to improve understanding of the natural course of AIS and the usefulness of HRQoL measures in determining treatment decisions. We predict that increasing ODI scores will correlate with age, curve size, curve location and progression to surgery. Additionally, we predicted that SRS-22r scores in our study population would show no difference between age-gender matched controls.

Methods: All unoperated adult patients with a diagnosis of AIS seen at a tertiary deformity clinic from 2008-2018 were identified using ICD coding and reviewed. Variables collected included: general demographics, cardiac, pulmonary, endocrine, and psychological comorbidities, family history of scoliosis, curve size, curve location, curve major, visual analog pain score, ODI and SRS-22r scores, and previous treatment. ODI and SRS-22r scores were analyzed across three separate age groups: 20-39yrs (G1), 40-59yrs (G2), and ≥60yrs (G3). Continuous variables were analyzed and compared using means, standard deviations, and variances and categorical variables were compared using frequencies. For ODI analysis we used ANOVA for comparison between groups, Pearson correlation to assess linear relationship with patient characteristics, and chi-square analysis to determine score frequency of ≥30 within groups. For SRS-22r, mean domain scores were analyzed for each age-gender stratified group (G1-G3). ANOVA and Kruskal-Wallis tests were used to compare continuous variables between

all three groups and one sample t-tests were used to compare our sample means to published normative data. Analysis comparing presurgical SRS-22r domain scores and ODI in patients who did and did not go on to have surgery was also performed using T $\geq 50^{o}$ and/or TL $\geq 40^{o}$ as a cutoff for surgical indication.

Results: A total of 249 patients (84% female and 16% male) met inclusion and exclusion criteria and were identified for analysis. 214 patients (84% female) had an ODI score. Mean ODI score increased with each age group ($p<.001$). ODI scores had a positive linear correlation with age, BMI, and curve size ($p<.001$). 200 patients (83% female) had an SRS-22r score. The only domains showing no difference between age-gender matched normative data for SRS-22r were function in G1 females and all groups for male; mental health in G3 females and G2 males; self-image in G2 males ($p>.05$). Pain was worse in all age-gender matched domains ($p<.05$). Of the 249 patients in the study, approximately 10% went on to have surgery. In patients with surgical sized curves noted in the methods, no difference was seen in age or curve size between surgical and non-surgical patients, however ODI and SRS-22r scores (excluding mental health) were significantly worse ($p\leq.01$).

Conclusions: Patients with AIS have SRS-22r scores that are lower than age-gender matched controls in most domains. ODI had a positive linear correlation with age, body mass index, and curve size. Furthermore, 10%, of adults with surgical sized curves (Thoracic $\geq 50^{o}$; Thoracolumbar $\geq 40^{o}$) who sought evaluation for scoliosis pursued surgery. Patients who did go on to have surgery, reported worse preoperative HRQoL scores than their non-surgical counterparts. These results can help healthcare providers when counseling patients and families concerning treatment decisions.

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Chapter 1: Literature Review

Definition & Diagnosis

Scoliosis is a lateral curvature of the spinal vertebrae within the coronal plane (1) and is derived from the Greek word *skoliosis*, meaning crookedness (2). Scoliosis can cause lateral curvature in the coronal plane, axial rotation in the transverse plane, and an interruption of the normal curvature seen in the sagittal plane (3). Scoliosis can be structural or functional in nature (muscle tone or limb asymmetry) (3). The focus of this paper is structural scoliosis. When the cause of scoliosis is unknown, it is determined to be idiopathic (4). Neuromuscular disease, congenital bony deformity, or syndromic disorders can also cause scoliosis. Idiopathic scoliosis, which comprises 80% of all scoliosis diagnoses, develops during childhood and can be further broken down into infantile, juvenile, adolescent and adult idiopathic scoliosis based on age at diagnosis (2,3,5). Adolescent Idiopathic Scoliosis (AIS) represents the majority of idiopathic scoliosis patients (2,6,7). Definitive diagnosis is made by upright radiographic imaging showing a curve angle (Cobb angle) measuring greater than 10 degrees (1,3,5). Patients may initially be screened with an Adam's forward bend test in combination with scoliometer measurements prior to imaging (5).

Epidemiology

The prevalence of AIS in the general population is estimated to be between 1 and 4% (2,3,6) . Of those diagnosed with AIS, only 10% will require treatment (3,8,9) and it is estimated that only 0.1-0.3% will require surgery (3,10). The ratio of females to males initially affected by scoliosis, ranges from 1:1 up to 3:1 (2). However, the risk of progression, and therefore the need for treatment, is ten times higher in females than in males (8). The majority of AIS curves present as a right thoracic curve (2,5). Curves presenting as a left thoracic curve may indicate a

more serious pathology and should prompt the physician to consider spinal cord tumors, malformations of the spine, or neuromuscular disorders (5).

Treatment

Treatment for AIS can be divided into surgical and non-surgical (conservative) management both of which aim to decrease progression of the spinal curve and prevent adverse sequelae. Conservative management predominantly includes observation and/or bracing with the majority of curves requiring no intervention (4). Conservative treatment is meant to prevent curve progression while the goal of surgical treatment is curvature correction (4,7). Indications for operative versus non-operative treatment are based on measurements of bone maturity, curve angle, and risk of future progression. Skeletal maturity, represented by the Risser score, is graded on a 0 to 5 scale with 0 being immature and 5 being fully mature (2,3). Risser score is a measure of the percent of calcification from the lateral to the medial portion of the iliac apophysis (2). Pelvic radiographs are used to measure the progression of ossified bone with 0 representing no calcification of the apophysis and 5 representing full calcification and complete fusion of the iliac apophysis (2). A lower Risser grade correlates with a higher risk for curve progression and higher need for bracing and surgical treatment. Curve progression is measured every six to twelve months using scoliosis films. A curve that does not increase in size can be monitored closely, while a curve that increases by 6 degrees is considered progressive (3). The degree of curvature is a common way of reporting and understanding the severity of a scoliosis curve. A Cobb angle measuring less than 20 degrees tends to be observed, while curves greater than 45 to 50 degrees are considered for surgical correction. Curves from 25-45 degrees in patients with considerable growth remaining are candidates for brace treatment (3).

Factors that must be taken into account for brace management of AIS include: curve magnitude, curve type and location, remaining growth potential, cosmetic appearance, and patient related psychosocial factors (7). Bracing is recommended for skeletally immature patients (Risser 2 or less) with a curve between 25-45° (7). Rigid bracing is the most common form of non-surgical treatment for scoliosis (11). Thoracolumbar orthoses (TSLO), including the Boston, Charleston, and Providence braces, are commonly selected and are suitable for curves with an apex at T7 or lower (7). Proper counseling must be done when considering a brace as the treatment requires many hours of brace-wear and compliance by the patient (7). A landmark multicenter clinical trial performed by Weinstein et al. definitively showed the efficacy of bracing in preventing high-risk patients with AIS from reaching the surgical threshold of a curve with a Cobb angle of ≥50° (11,12). They also found a positive association between hours of brace wear and rate of treatment success. The study was stopped early due to the clear efficacy of bracing (11).

Surgical treatment is generally recommended for patients with curve magnitude greater than 45 degrees who are Risser 2 or less and considered for curves greater than 50 degrees in patients who are Risser 3 or greater (7). The goal of surgical treatment is to arrest curve progression while also improving alignment and spinal balance. It is achieved by placing spinal instrumentation to correct and stabilize the spine while performing a concomitant arthrodesis of the bony elements (7). Instrumentation techniques have evolved over the years pioneered by surgeons such as Harrington (13) and Luque (14) and has now advanced to multiple anchor systems with planned integration of screws, hooks and even wires (15). Arthrodesis can be performed anteriorly, posteriorly, or both depending on the skeletal maturity, curve type, magnitude, and surgeon skill set (7). A classification system, known as the Lenke classification,

was developed to accurately classify curves and to serve as a template to perform selective fusions of the spine. The Lenke classification is composed of the triad of curve type, lumbar spine modifier (A, B, C) and a sagittal thoracic modifier (-, N, +) (16). Lenke found that selective thoracic or thoracolumbar/lumbar fusions of the major curve can be performed successfully even if the minor curve deviates from the midline and can optimize mobile segments of the spine (16). Another prospective non-randomized study performed by Newton et al. in 2013 compared the outcomes of open anterior spinal fusion, thoracoscopic anterior spinal fusion, and posterior spinal fusion in AIS patients with thoracic curves. They concluded that all three approaches produced similar satisfactory outcomes in most patients, however, the open anterior group had no clear advantage over the other two treatments with a possible reduction in pulmonary reduction (17). Regardless of the surgical approach, factors that must be considered in preoperative planning include level of skeletal maturity, curve flexibility, spinal balance, curve type and magnitude.

Etiopathogenesis

The etiopathogenesis of AIS is complex and a single factor responsible for AIS has not been identified. The multitude of theories described in the literature suggest a multifactorial etiology. Studies have suggested the role of genetic factors, hormonal factors, neurological abnormalities, collagen and elastic factors as well as biochemical factors and growth abnormalities. Genetic factors have been proven to play a role in multiple studies and indicate 11% of first-degree relatives are affected, as well as 2.4% and 1.4% of second and third-degree relatives, respectively (18). These same trends have also been seen in monozygotic twin-concordant studies (19). Numerous genes have been implicated in the development of AIS, including a Japanese study in which genome-wide significant variants near LBX1 were identified

in female patients with AIS (20). A study performed by Nowak et al. analyzed TGF-β responsive genes in the transcriptomes of patients with AIS and suggested there was an overrepresentation of genes localized in the extracellular region of curve concavity (LTBP3, LTB4, ITGB4 and ITB5) (21). This finding may suggest the extracellular region of paravertebral muscles as a possible target for future molecular research. Additionally, a study done in 2013 implicated G protein-coupled receptor 126 (GPR126) in the development of AIS (22). Results of many candidate-gene analysis studies have excluded fibrillin 1 and 2, collagen type I and II, elastin, aggrecan, and various heparan sulfotransferases as genetic causes of AIS (4). Despite the efforts of many, no single gene has been identified in the development of AIS suggesting that AIS is a complex genetic disorder. Furthermore, the relationship between genetics and environmental factors must also be considered.

The most studied hormonal factors that have been implicated in the development of AIS are melatonin and calmodulin. Melatonin signaling dysfunction was described by Moreau et al. and a molecular classification system was developed for patients with AIS according to their differential G_i-coupled receptor signaling response (23). This was further supported in a 2010 study that linked the melatonin signaling dysfunction with G_i-coupled receptor signaling dysfunction (24). However, research regarding melatonin's role in AIS remains controversial. Morcuende et al. found no mutations in the coding region for several melatonin receptor genes in patients with familial AIS (25). In a pinealectomy model using primates, one study found that scoliosis could not be produced despite the suppression of melatonin in a 28-month period of observation (26). Additionally, melatonin levels are known to diminish in sleep disorders, but there has been no evidence to suggest an association with AIS and sleep disorders suggesting that scoliosis does not result simply from absence of melatonin but possibly through more complex

signaling (4). Another hormone, calmodulin, has been shown to have a 2.5- to 3-fold increased activity in platelets (27). Cohen et al. indicated that platelet calmodulin level could be a better indicator for progression of the curvature than the Risser sign alone (27). The role of calmodulin in the etiopathogenesis of AIS has yet to be fully defined.

Collagen and elastic fiber dysfunction have also been theorized in the etiology of AIS. In 1994, Hadley-Miller et al. found elastic fiber abnormalities in the spinal ligaments in patients with AIS, when compared to healthy individuals (28). Growth abnormalities have also been postulated to the development of AIS. Chu et al. showed the morphological features of relative spinal cord tethering in AIS using images supporting the hypothesis that uncoupled neuro-osseous growth between the vertebral column and spinal cord may contribute to the development of AIS (29). Porter hypothesized that anterior structures grow more rapidly than posterior structures and with bending forward, the vertebral bodies at the apex tend to move forward by rotating to the side (30). This is supported by the association of AIS with hypokyphosis in the sagittal plane (30).

Natural Course of Idiopathic Scoliosis

As discussed above, idiopathic scoliosis can present in various stages of the lifecycle associated with periods of rapid growth. Development of scoliosis between the age of 6 to 24 months, 5 to 8 years, and 10 to 14 years of age corresponds with infantile, juvenile, and adolescent idiopathic scoliosis respectively (3). However, it is often more difficult to tell if juvenile or adolescent scoliosis began at an earlier age and likely there may be a blend between the classifications (10). At the start of puberty, the risk of curve progression is highest (3). Longitudinal axial growth following elongation of the limbs is the period of greatest curve advancement (3). In girls, menarche signals a gradual decrease in curve progression (3). The

potential for scoliotic curve progression is significantly reduced following puberty and completion of bone growth. Potential complications of idiopathic scoliosis include increased back pain, decreased pulmonary function, and psychosocial complications. Mortality has not been shown to be increased in AIS despite notable misinformation stated in very early studies (4,31–33). The exception is in severe cases of scoliosis with curves greater than 110 degrees and a pulmonary vital capacity less than 45% (34).

Significance of Health-Related Quality of Life

Recent interest has increased concerning long-term quality of life in AIS. Health Related Quality of Life (HRQoL) questionnaires such as the Scoliosis Research Society-22r (SRS-22r) and the Oswestry Disability Index (ODI) have become the standard for assessment of disorders of the spine (35). Danielsson described HRQoL in 2001 as, "a subjective multidimensional construct that captures the impact of health status, including disease and treatment, on three core domains: physical, psychological, and social functioning" (36,37). Scoliosis typically does not increase mortality but can be disfiguring or burdensome to certain patients. Treatment may require a multi-step process over a lengthy period that subjects the patient to bracing or surgery. Therefore, questions concerning function, psychological well-being, and social self-image are important in the long-term treatment associated with AIS (36). HRQoL assessment can be advantageous as it provides additional patient information beyond that obtained objectively through physical exam, labs, and imaging. Evaluating patient reported HRQoL is inexpensive and often complements objective data offering a more holistic view of a patient (36).

Studies focusing on analyzing health-related quality of life in patients with AIS are limited and conflicting. One study found that psychological well-being and function is quite good in patients with AIS 20 years after surgery or brace treatment, but did not look at patients

who underwent observation (36). Ascani et al. reported the opposite, however, with approximately 20% of their patient population experiencing psychological disturbance (4,38). In a review of AIS and the relevant literature concerning HRQoL performed in 2013, Danielsson was unable to determine that quality of life or function was significantly different from the normal population. Additionally, cosmetic problems did not seem to be a problem for most patients (32). Asher et al. used the SRS-22 patient questionnaire to assess the change associated with surgical treatment (39). This study found that function and degree of pain returns to near baseline by 6 months, self-image is significantly improved by 3 months, while mental health is not significantly affected (39). In an attempt to promote further research using HRQoL data, Baldus et al. collected SRS-30 age-gender normative data for comparison purposes concluding that clinicians must be mindful of age-gender differences when assessing deformity populations (35). Future studies can focus on the generational decreases noted in the older adult volunteer scores and may be used to interpret observed score decreases in patient cohorts at long-term follow-up (35).

Chapter II: Introduction

Adolescent idiopathic scoliosis (AIS) is diagnosed in approximately 1% to 4% of all children (2–5,10,32), yet questions still exist concerning the long-term complications and quality of life measures in those who are affected. Original longstanding studies concerning idiopathic scoliosis described a life of pain, disability, psychosocial complications, and cardiorespiratory decline (40–42). However, these studies failed to completely exclude congenital scoliosis and scoliosis due to secondary causes (40–42). More recent studies indicate that adolescents diagnosed with idiopathic scoliosis go on to lead normal functioning lives with minimal differences in quality of life (4,5,31,32).

Though some studies have shown that patients living with AIS tend to report increased pain, a preponderance of those patients reported only mild to moderate rather than severe pain (31,32). With respect to cardiorespiratory dysfunction, a natural history review on AIS performed by Danielsson in 2013 concluded that patients are only at increased risk of pulmonary symptoms if their curve size is greater than 80 degrees or if they have significant coronal rotation (32). Scoliotic curves with Cobb angle >80 degrees were associated with an increased risk of shortness of breath (10). A Cobb angle >110 degrees in conjunction with vital capacity estimate of <45 percent-predicted are associated with increased risk of respiratory failure (32,34). Results concerning mental and social health have shown differing results with some reporting no increased disturbances (31,32) and other studies indicating that scoliosis does affect mental health in women with curves >40 degrees (38). Furthermore, untreated scoliosis does not appear to prevent employment, marriage, or pregnancy. Additionally, pregnancy does not increase the risk of progression in women with scoliosis (10,43,44). Regardless of a potential for pain, respiratory, or psychosocial disability, no natural history study pertaining to idiopathic scoliosis

alone, has shown an increased rate of mortality (10,31,32). A 50-year follow up study performed by Weinstein et al. in 2003 showed similar estimated survival probability of 0.55 in idiopathic scoliosis compared to 0.57 in unaffected adults (31).

With a reduced concern for mortality related to AIS, research should emphasize HRQoL measures in AIS to further classify the natural history of disease. This would allow physicians and patients to make a more educated decision regarding treatment strategy. Presently, the decision to treat scoliosis conservatively or surgically is based on several factors, notably radiographic curve size (no less than 45 degrees), risk of progression, and pain unresponsive to conservative management (4). Curve sizes exceeding 45 to 50 degrees are considered for surgery with a range of 50 to 80 degrees seen as a grey zone according to Danielsson (32). Factors that place a patient at risk of curve progression include gender with females possessing a ten-fold greater risk, magnitude of curve, skeletal maturity, and apex location with thoracic curves more likely to progress (4,5). Curves over 50 degrees in skeletally mature patients have been shown to continue progressing at an estimated rate of 0.5 to 1 degree per year (45).

The goal of treatment is to reduce complications and increase quality of life. Conservative treatment aims to prevent curve progression while surgery aims to correct and maintain the curve (4). Several HRQoL tools have been created and have become a reasonable means for assessing short and long-term outcomes regardless of treatment history. The Scoliosis Research Society (SRS) Outcome Instrument designed by Haher et al. is a simple questionnaire designed for assessment of function, pain, mental health, and social image (46). The SRS-22, and later SRS-22r, were modifications of the original instruments that improved its psychometric qualities and represent the final version of the questionnaire (39,47–50). The Oswestry Disability Index (ODI), first published by Fairbank et al. (51) is a validated questionnaire that quantifies

disability due to back pain. These instruments are suitable for evaluating patient reported outcomes and provide an opportunity for measuring outcomes in clinical spine research.

To better understand the natural history of idiopathic scoliosis in adulthood, we conducted a study using HRQoL data (ODI and SRS-22r questionnaires) in adult patients previously diagnosed with AIS. Our overall objective was to further establish the impact of untreated AIS in adulthood. The underlying rationale for this project was to improve understanding of the natural course of AIS and the usefulness of HRQoL measures in determining treatment decisions. We hypothesized that ODI scores would correlate with age, curve size, curve location, and progression to surgery. Additionally, we hypothesized that SRS-22r scores would be similar to age-gender matched controls and those with worse scores (high ODI and low SRS-22r) would progress to surgical treatment. Our primary outcome measures were surgical rate, ODI scores, and SRS-22r domain scores.

Chapter III: Methods

Study Approval

This study was approved by the Institutional Review Board at the University of Kansas Medical Center (KUMC) from 9/4/2018 to 9/3/2019 with a waiver of HIPAA authorization and informed consent (IRB STUDY00142851).

Setting

This was a retrospective cross-sectional study conducted at a single-center tertiary care hospital (The University of Kansas Hospital (TUKH)). The Marc A. Asher, MD, Comprehensive Spine Center is located within TUKH and sees a high volume of spine patients, including those with AIS.

Participants

Study participants consisted of all unoperated adult patients with a diagnosis of AIS seen at a tertiary deformity clinic from 2008-2018. Participants were retrospectively identified using ICD-9 and 10 diagnosis codes for adolescent and acquired scoliosis. ICD-9 codes included 737.3 and 737.43. ICD-10 codes included M41.0 through M41.39. Patients were then narrowed down based on inclusion and exclusion criteria identified through individual chart review.

Inclusion criteria included patients who were ≥20 years of age with a diagnosis of adolescent idiopathic scoliosis confirmed by radiographic evaluation and patient history. On radiographic assessment, patients were required to have at least one thoracic (T) or thoracolumbar (TL) curve, >10 degrees, with an apex above L2 vertebrae. Patients with scoliosis secondary to neuromuscular disease or syndromes were excluded. Scoliosis determined to be degenerative in nature were identified and excluded. Variables collected were general demographics, cardiac, pulmonary, endocrine, and psychological comorbidities, family history of

scoliosis, curve size, curve location, curve major, visual analog pain score, ODI and SRS-22r scores, and previous treatment.

Statistical Analysis

ODI and SRS-22r scores were analyzed across three separate age groups: 20-39yrs (G1), 40-59yrs (G2), and ≥60yrs (G3). Data cleaning and statistical analysis were performed using SPSS® Statistics Version 25 (© IBM Corporation, Armonk, NY, USA). Continuous variables were analyzed and compared using means, standard deviations, and variances and categorical variables were compared using frequencies. A two-tailed hypothesis test with alpha level of .05 was used to determine significance.

Analysis for ODI data.

ODI total scores were calculated and analyzed across each age group (G1-G3) using ANOVA. Pearson correlation coefficient was performed to assess for a linear relationship between ODI score and age, BMI, or curve size. ODI score frequency ≥30 was analyzed for each group using Chi-square analysis. We chose 30 as a threshold for severe disability based on a study performed by Park et al. which recommended 30 as a cutoff value for safe inpatient discharge in patients with back disability (52). Subgroup analyses were also done comparing thoracic and thoracolumbar major curves with respect to curve size and ODI score using two sample t-test to compare means. Pearson's correlation was also done for ODI score with respect to T vs TL major curves. Analysis using two sample t-test comparing ODI scores in patients who did and did not progress to surgery using T $\geq 50^{o}$ and/or TL $\geq 40^{o}$ as a cutoff for surgical indication was also performed.

Analysis for SRS-22r data.

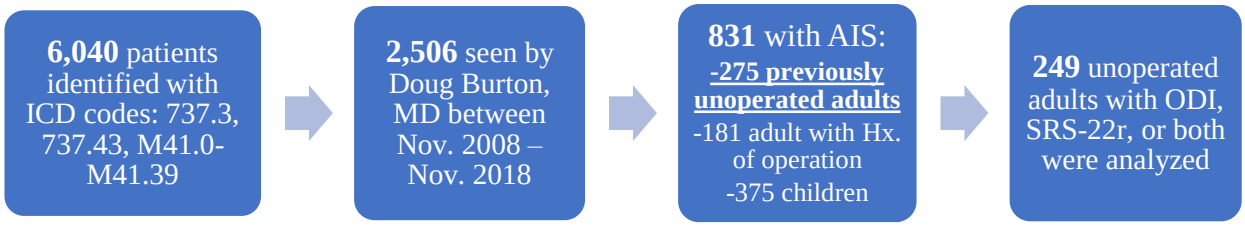
SRS-22r domain scores were calculated including function, pain, self-image, mental health, satisfaction with management, and total. Mean scores were analyzed for each age group (G1-G3). Each group was further subcategorized by gender. ANOVA and Kruskal-Wallis tests were used to compare continuous variables between all three groups and one sample t-tests were used to compare our sample means to published normative data. Analysis comparing SRS-22r domain scores in patients who did and did not go on to have surgery was also performed using similar criteria as seen above for ODI analysis.

Chapter IV: Results

Cohort Flow Diagram

6,040 total patients were identified using ICD coding. The cohort was narrowed down to 2,506 after sorting patients seen by Douglas Burton, MD at least once during the 10-year period from November 2008 to November 2018. All 2,506 patients were then individually reviewed via identified electronic medical records, keeping only the patients determined to have idiopathic scoliosis, resulting in 831 patients. Of those 831 patients, 275 patients fit the study criteria of adults (≥20 years of age) with a diagnosis of AIS who received no prior surgical treatment. 26 of those 275 patients did not have an ODI or SRS-22r score of which only 1 of the 26 patients received surgical treatment. 249 patients had either an ODI score, SRS-22r score, or both and represent the cohort we studied.

Figure 1. Cohort Determination



General Cohort Characteristics

A total of 249 patients met inclusion and exclusion criteria and were identified for analysis. Our cohort was 84% female and 16% male with an average age of 41 years. Our study population was 88% Caucasian with the remaining percentage distributed between African American (5%), Hispanic (3%), and other (4%). Of the 249 patients, 214 patients had an ODI and 200 had an SRS-22r score. 17 (7%) patients ultimately required a surgical procedure as an adult. A complete list of patient characteristics and demographics can be seen in Table 1 below.

Table 1. Baseline Demographics

Demographics	**Entire Cohort** (n=249)	**Age: 20-39** (n=130)	**Age: 40-59** (n=66)	**Age: 60+** (n=53)
Age (Mean)	41	26	49	68
Gender:				
F	209	102	60	48
M	40	28	6	5
Race:				
White	221	110	60	51
Black	12	7	3	1
Hispanic	6	4	1	1
Other	10	8	2	0
BMI (Mean)	25.5	24.7	26.6	25.9
Medical Hx:				
Depression	15	6	3	6
Anxiety	16	11	2	3
Both	24	16	5	3

Results for ODI Analysis

214 patients (84% female) had an ODI score and were included in this analysis. Mean ODI score increased with each age group ($p<.001$). ODI scores had a positive linear correlation with age, BMI, and curve size ($p<.001$). Patients with an ODI score ≥30 were as follows: G1= 17/108; G2= 20/60; G3= 25/46. The percentage of scores <30 for G1, G2, and G3 was 84%, 67%, and 46% respectively. Comparing frequency of <30 to ≥30 showed significance within each group (<.001) with G1 and G2 containing a greater number of patients below 30. When comparing T and TL cobb angle, there was no difference between curve size (47.7^o vs. 47.7^o, $p=.988$), however, mean ODI score was significantly different (T=20.07; TL=25.02, $p=.018$). ODI showed a positive linear correlation with T cobb angle (Pearson $r=.235$, $p=0.028$) and TL cobb angle (Pearson $r=.236$, $p=0.005$). Among pts with T ≥50^o and/or TL ≥40^o, only 13/127 (10%) patients underwent surgery. Among the 127 individuals with "surgical-size" curves, no difference in mean age or cobb angle was seen between surgical and non-surgical patients. ODI

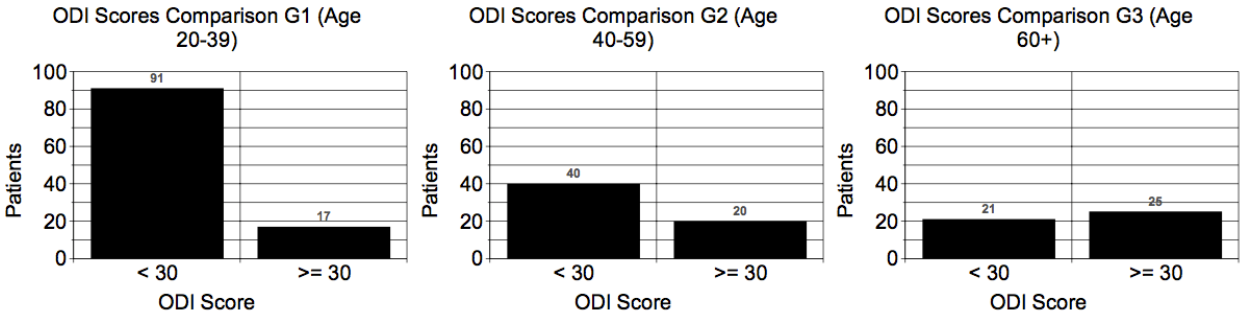
was, however, significantly higher in surgical (mean: 46.9) vs. non-surgical patients (mean: 22.8), (p<.001). Table 2 summarizes important data related to ODI analysis.

Table 2. ODI Outcome Data

	Age 20-39 (n=108)	**Age 40-59** (n=60)	**Age 60+** (n=46)	**p**
ODI Outcomes				
Raw ODI Score				
<30	91 (84%)	40 (67%)	21 (46%)	
≥30	17 (16%)	20 (33%)	25 (54%)	
Avg. ODI Score	18.34	24.43	32.15	<.001
	Thoracic (T)	**Thoracolumbar** (TL)		**p**
T vs TL Cobb				
Cobb Major (#)	88	126		
Avg. Cobb Size	47.74º	47.7º		.988
Avg. ODI Score	20.07	25.02		.018
	Non-Surgical (n=114)	**Surgical** (n=13)		**p**
Surgical Curves[1] **(T ≥50º/TL ≥40º)**				
Percent	90%	10%		
Age	47	52		.34
Avg. Cobb Size				
T	54.7º	54.75º		.995
TL	55.6º	57.3º		.689
Avg. ODI Score	22.8	46.9		<.001

[1] Surgical curves pertain to the estimated degree that a surgeon may begin to consider operation based on Cobb major location (Thoracic vs Thoracolumbar).

Figure 2. ODI Score Comparison (< vs ≥ 30)



Results for SRS-22r Analysis

200 patients (83% female) had an SRS-22r score and were included in this analysis. G1 had 108, G2 had 52, and G3 had 40 patients. Mean scores for the entire cohort were: function=4.02, pain=3.18, self-image=3.18, mental health=3.76, and total=3.46. When analyzing across age groups, there was a significant difference between groups for function ($p=.001$), pain ($p=.008$), self-image ($p=.016$), and total ($p=.02$); there was no difference in mental health scores ($p=.536$). In comparison to each age-gender normative data group, our cohort had worse scores for pain in all groups ($p<.05$). Function was significantly different in females age ≥40 (G2, G3), however, no difference for females in G1 or males of any age. Mental health scores were worse for females in G1 and G2 ($p<.001$) and males in G1 and G3 ($p<.05$). For self-image and total domains, females in all groups and males in G1 and G3 reported worse scores ($p<.05$). Among patients with T cobb angle ≥50º and/or TL Cobb ≥40º, only 12 out of 118 (10%) patients underwent surgery. Among those 118 patients with "surgical-size" curves, there was no difference in curve size, age, or BMI, but there were significant differences in function ($p<.001$), pain ($p=.001$), self-image ($p=.01$), and total ($p=.002$) SRS domain scores with surgical patients reporting worse or lower scores in each domain. Tables 3 and 4 summarize important data related to SRS-22r analysis.

Table 3. SRS Scores Compared to Age-Gender Normative Data

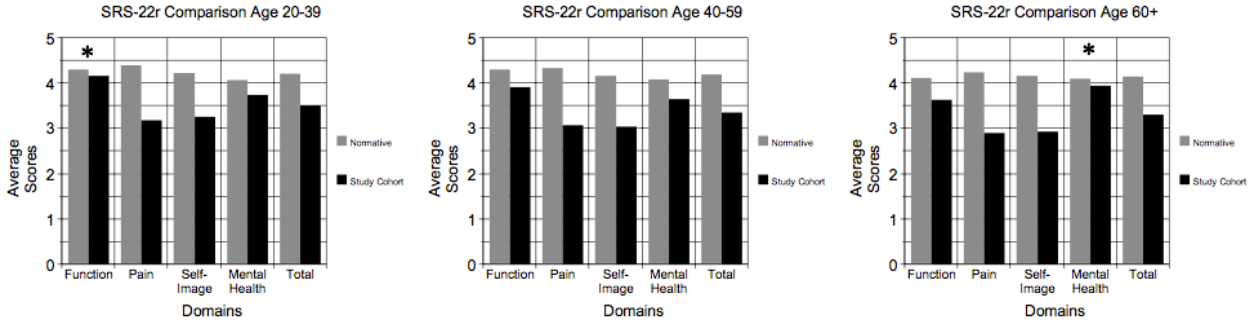
	Age 20-39		Age 40-59		Age 60+	
	F (n=84)	**M** (n=24)	**F** (n=47)	**M** (n=5)	**F** (n=36)	**M** (n=4)
Function						
Mean	4.16	4.32	3.91	3.92	3.63	4.05
Avg (F & M)	4.2		3.91		3.68	
Normative	4.3	4.44	4.3	4.29	4.11	4.18
Pain						
Mean	3.18	3.91	3.07	2.96	2.89	2.48
Avg (F & M)	3.35		3.06		2.85	
Normative	4.4	4.57	4.33	4.4	4.23	4.4
Self-Image						
Mean	3.25	3.55	3.04	3.08	2.93	3.25
Avg (F & M)	3.32		3.05		2.96	
Normative	4.22	4.46	4.16	4.25	4.16	4.27
Mental Health						
Mean	3.74	3.82	3.64	3.84	3.94	3.43
Avg (F & M)	3.76		3.66		3.89	
Normative	4.06	4.33	4.08	4.22	4.09	4.28
Total						
Mean	3.51	3.79	3.35	3.34	3.3	3.23
Avg (F & M)	3.57		3.35		3.29	
Normative	4.21	4.43	4.19	4.27	4.14	4.28

Table 4. SRS-22r Analysis of Surgical Sized Curves

	Non-Surgical (n=106)	**Surgical** (n=12)	**p**
Surgical Curves[1] **(T ≥50º/TL ≥40º)**			
Percent	90%	10%	
Age	46	51	.319
Avg. Cobb Size			
T	53.3º	54.75º	.814
TL	54.1º	58.4º	.277
Avg. SRS Score			
Function	4.05	2.83	<.001
Pain	3.22	2.29	.001
Self-Image	3.09	2.49	.01
Mental H.	3.81	3.7	.64
Total	3.46	2.83	.002

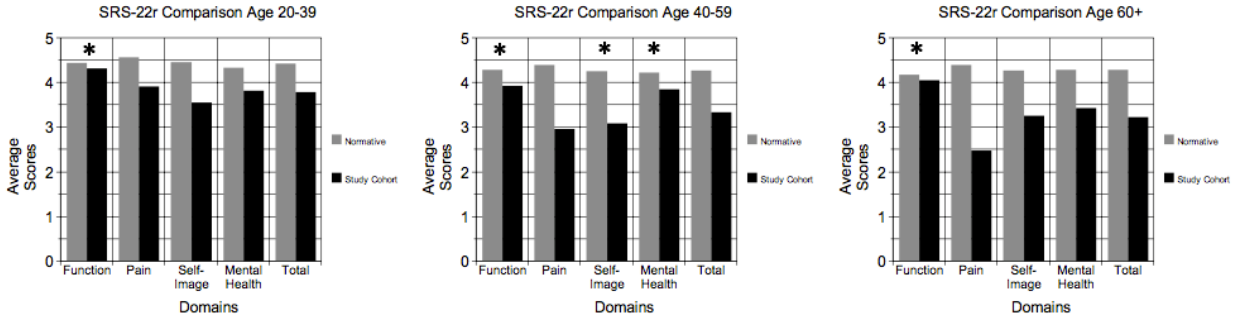
[2] Surgical curves pertain to the estimated degree that a surgeon may begin to consider operation based on Cobb major location (Thoracic vs Thoracolumbar).

Figure 3. SRS-22r Scores Compared to Age-Gender Normative Data -Female



* indicates *no* age-gender difference between our cohort and normative data

Figure 4. SRS-22r Scores Compared to Age-Gender Normative Data -Male



* indicates *no* age-gender difference between our cohort and normative data

Chapter V: Discussion

Despite early literature suggesting lifelong complications and morbidity, later studies showed that adolescents diagnosed with AIS can lead healthy, productive lives with normal life-expectancy (31). While considerable advances in assessment and treatment of idiopathic scoliosis have occurred, advancements in the understanding of natural history and quality of life in AIS are lagging. With no evidence to support increased mortality, focus should be placed on optimizing or personalizing treatment strategies to provide the best quality of life. Within the current literature, there is a dearth of information pertaining to long-term quality of life measures in adults treated conservatively in childhood for AIS. Our purpose was to expand the current knowledge on natural history of AIS and provide further information that can be utilized by spinal deformity physicians when counseling patients and their families.

In this study, we measured two validated HRQoL questionnaires (ODI and SRS-22r) in adults across three separate age groups: 20-39, 40-59, and ≥ 60 to estimate quality of life expectations and determine their usefulness in predicting progression to surgery. The results of our study can be used to provide estimates for quality of life predictions and may present as a guide for future hypothesis generating research in scoliosis. An important finding within our data is the correlation with worsening HRQoL scores and the decision to proceed with surgery. In our study population of unoperated adults with AIS, of those with Cobb angles large enough to be considered for surgery (Thoracic $\geq 50^{o}$; Thoracolumbar$\geq 40^{o}$), only 10% went on to receive surgery. When comparing preoperative ODI and SRS-22r scores in those who pursued surgery to those who did not, we found that patients requiring surgery reported significantly higher ODI and lower SRS-22r scores (except mental health) than their non-surgical counterparts despite no difference in age or curve size between groups. These findings aligned with our theory that

worsening scores would correlate with progression to surgery. Attempts to seek out literature discussing this topic or the topic of HRQoL tools as correlates for surgery were unsuccessful. Regardless, these results reinforce the use of quality of life measures in scoliosis treatment.

In our analysis comparing SRS-22r data to age gender normative scores, we found that our cohort had slightly worse scores in most domains than unaffected peers. These results, for most age-gender domains, failed to prove our hypothesis that unoperated adults with AIS have similar scores to age-gender matched controls. However, some sub-domains, primarily in our male cohort, did not show any difference. The sub-domains that were similar to age-gender data can be seen in Figures 3 and 4 above. These results seem to align with several current studies reporting similar lower scores. A recent study by Larson et al., which is currently accepted and in press, concluded that AIS patients report scores that are approximately 10% worse than population-based controls (53). Despite worse scores, most patients have been shown to function at near normal levels (10). Function was not different in males of any age and younger females in our population. Additionally, most natural history studies agree that pain is increased in AIS when compared to controls (10). Self-image scores vary with some studies showing decreases in body image during treatment with subsequent return to normal and other authors reporting a significant limitation in social activity due to back deformity (10,36,54). Weinstein et al. demonstrated that AIS patients do differ significantly from controls with worse scores than unaffected controls (31). Our results generally agree with those found by Weinstein and others, but one caveat must be noted concerning our self-image scores. In our comparison to age-gender normative data, we used SRS-30 data from Baldus et al. which includes one extra question asking the patient to rank their self-image on a scale (35). The rest of the added questions in the

SRS-30 are for post-surgical patients only which does not apply to the data collected in our study and does not affect the sub-domains of function, pain, and mental health.

Studies concerning mental health in scoliosis have produced differing results. One study concluded that deformities are better tolerated in older populations aligning with findings regarding the female population in our study (43). Another study found that women with thoracic curve size greater than 40 degrees were at greater risk for psychological disturbance with 39% of that population experiencing psychological complications (38). Further differences were concluded by Weinstein in 2003 following a 50-year natural history study where they found no difference in mental health between untreated idiopathic scoliosis and controls (31). Mental health was the only sub-domain that was not significantly different between patients that did and did not progress to surgery in our study. With the conflicting results in mental health across different studies, it proposes the question of whether mental health arises de novo in the setting of scoliosis as a separate disease process or if it is initiated and truly worsened by scoliotic deformity.

Additional findings concerning ODI analysis aligned with our SRS-22r data and that of the literature. ODI had a positive correlation with age, BMI, and curve size which would be expected both intuitively and based on literature. ODI scores also showed differences when considering curve location. Patients with a thoracolumbar curve apex had worse scores (25 vs. 20) than those with thoracic major curves. This confirmed our hypothesis that ODI correlates with age, curve size, and curve location. A population-based cross-sectional study done in 2016 was able to show the effect of mood disorders on low back pain in males concluding an increase in low back pain and/or disability in the setting of obesity and emotional disorder (55). They suggest evidence of a biopsychosocial interaction that intertwines weight, disability, and

psychosocial perceptions leading to increased pain (55). Using an ODI score of 30 as a cutoff for severe disability (52), we found that the majority of patients had scores lower than 30 especially in younger individuals. In both G1 and G2, comprising adults from age 20 to 59, 131 out of the 168 patients reported an ODI score below 30, while in G3, adults age ≥60, only 21 out of the 46 patients had a score below 30.

Limitations

There are several limitations in this study, mainly due to the observational and retrospective study design. Retrospective studies have inherent inadequacies regarding confounding and bias that are harder to remove than when conducting a prospective study. Retrospective studies are, however, beneficial in generating hypotheses and reducing cost especially when long term follow up may be difficult (10). Limitations also exist due to a cross-sectional design where disease status and measurement outcomes are measured at the same time. Due to this, no causal or temporal relationship can be assessed using our data (56). Furthermore, cross-sectional design is prone to bias (56). Selection bias may be present since patients seeking out spinal deformity care may have worse disease or a worse outlook on disease than those that choose not to pursue care. This may be considered a form of non-response bias typically seen in surveys since those electing to pursue scoliosis care may have different perceptions than those who chose not to pursue care. Additionally, patient reports of disability, dysfunction, pain, self-image, and mental health were assumed to be due to scoliosis and not concomitant disease or degeneration.

Chapter VI: Conclusion

This study provides quality of life and disability estimates in adult AIS patients who were treated conservatively as adolescents. The results demonstrate that patients with AIS have SRS-22r scores that differ from age-gender matched controls in most domains. They also highlight the correlation of ODI with age, body mass index, curve location, and curve size. Furthermore, only 10% of adults with surgical sized curves (Thoracic $\geq 50^{o}$, Thoracolumbar $\geq 40^{o}$) who sought evaluation for scoliosis pursued surgery. Patients who did go on to have surgery, reported worse preoperative HRQoL scores than their non-surgical counterparts. Pediatric deformity surgeons as well as primary care providers can use this information when counseling skeletally mature patients diagnosed with AIS and their families regarding the need for surgery or surgical evaluation.

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